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10/511,048	10/12/2004	Benoit Denizot	REGIM 3.3-039	6218

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EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
06/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,048	DENIZOT ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of Applicant's arguments and amended claims filed on 02/23/09 is acknowledged.

Applicants had elected species 6-trimethylammoniohexyl-1, 1-bisphosphonic acid to be prosecuted, however, the claim directed to elected species has been canceled by applicants.

Claims 8-13 are under prosecution to the extent they read on the elected species.

Rejections not reiterated herein have been withdrawn in view of Applicants amendments to claims.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

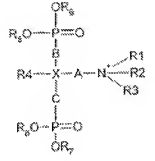
3. Claims 8-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The claims are drawn to: an oral hygiene composition with formula I

a polyphosphonate compound having a structure represented by formula I:



(I)

wherein:

R1, R2, R3, R5, R6, R7, R8 represent an atom of hydrogen or an alkyl or aryl group in C1 - C6, independently of each other;

X is a carbon C atom ~~or a nitrogen N atom~~;

A represents an alkyl or aryl group in C1 - C6, a carbonyl group or a hydrophilic group, B and C represent a chemical bond~~, an alkyl or aryl group in C1 - C6, a carbonyl group, or a hydrophilic group~~; and

R4 represents:

a hydrogen atom, an OH group, an alkyl or an aryl group in C1 - C6, ~~or a carboxylic acid in C1 - C6, a free doublet (if X is a nitrogen N)~~, or

a phosphonate with formula:

in which R9, R10 represent a hydrogen atom, or an alkyl or an aryl group in C1 - C6, independently of each other;

The breadth of the claims

The instant claims encompass composition comprising polyphosphonate with many substitutents hanging off of it.

The claims disclose various species with various substituents. The specification only provides preparation of one species. In the absence of guidance provided in specification, one skilled in the art would undergo undue experimentation while practicing the invention. The disclosure provides no guidance as how to prepare various claimed polyphosphonates with multiple substituents. The specification does not disclose starting material in preparation of each and every possible species.

The level of predictability in the art: Even when similar starting material is used under the same conditions the products obtained are different.

As stated in the preface to a recent treatise:

Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the

> impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor- intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work..... Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious). Dorwald F. A. Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

Thus synthesis of these compounds is unpredictable.

The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. Only limited substitutents on the compounds are made and disclosed. There are no compounds with every possible substituent, the availability of the starting material that is needed to prepare the invention as claimed is also at issue here. As per MPEP 2164.01 (b): A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. The Court in In re Ghiron, 442 F.2d 985,991,169 USPQ 723,727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. In re Howarth, 654 F.2d 103, 105,210 USPQ 689, 691 (CCPA 1981). There are no starting materials provided with respect to the various substituents. 7) The existence of working examples: The instant specification does not have any working examples with respect to the various substitutents as given above. The state of the art indicates that even when the reactants are similar, and the reaction conditions are the same, it is not necessary that it would form the same products.

State of the Prior Art and the level of skill in the art

The existence of working examples: The instant specification does not have any working examples with respect to the various substitutents as given above. The state of the art indicates that even when the reactants are similar, and the reaction conditions are the same, it is not necessary that it would form the same products.

The level of skill is very high.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

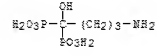
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Ali Vassem (WO 2000067708).

Vassem teaches oral dentifrice comprising a therapeutically effective amount of

phosphonic acid. The reference discloses oral dentifrice compositions comprising a therapeutically effective amount of estrogen or an estrogen-containing substance are provided. A variety of different methods of using the compositions., for example in the treatment or prevention of tooth loss or osteoporosis, are also provided, see abstract.

IT 66376-36-1, Alendronate
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral steroidal hormone compns. for prevention and treatment of tooth loss or osteoporosis)
RN 66376-36-1 ZCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis- (CA INDEX NAME)

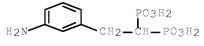


6. Claims 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 5,391,743.

The reference discloses a pharmaceutical composition containing quaternary nitrogen-containing phosphonate are prepared and used for prevention and treatment of abnormal calcium and phosphate metabolism such as such as osteoporosis, rheumatoid arthritis, osteoarthritis, dental calculus, plaque and gingivitis. Tetraethyl-3-(2,2-diphosphonoethyl)1-1(2-mercaptoethyl)pyridinium chloride (preparation is given)

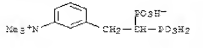
was hydrolyzed by refluxing in 6N HCl for 20 h under N, then the reaction mixture cooled and concentrated to obtain 3-(2,2-diphosphonoethyl)1-1(2-mercaptoethyl)pyridinium chloride (I). A capsule contained I 350.0, lactose 90.0, microcrystalline cellulose 60.0, and Mg stearate 1.0 mg. Phosphonate compounds were evaluated for bone resorption inhibition and mineralization in humans and animals, see abstract.

RN 154618-41-4 ZCAPLUS
CN Phosphonic acid, [2-(3-aminophenyl)ethylidene]bis- (9CI) (CA INDEX NAME)



RN 154618-21-0 ZCAPLUS
CN Benzenaminium, 3-(2,2-diphosphonoethyl)-N,N,N-trimethyl-, inner salt (CA INDEX NAME)

10/511048

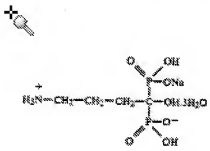


7. Claims 8 -13 are rejected under 35 U.S.C. 102(b) as being anticipated by

USP Gertz et al. (USP 5,270,365).

Gertz et al. teach a method for treating periodontal disease in mammals, including humans by administering a compound (which reads on the instant formula claimed).

ing an effective amount of 4-amino-1-hydroxybutyli-dene-1,1-bisphosphonic acid or a pharmaceutically ac-ceptable salt including the monosodium salt trihydrate (alendronate) of the formula:



See abstract. Various drug amounts are disclosed in claims 2-8.

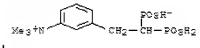
8. Claims 8 -13 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 5,760,021.

The reference discloses a pharmaceutical composition containing quaternary nitrogen-containing phosphonate are prepared and used for prevention and treatment of abnormal calcium and phosphate metabolism such as such as osteoporosis, rheumatoid arthritis, osteoarthritis, dental calculus, plaque and gingivitis. Tetraethyl-3-(2,2-diphosphonoethyl)1-1(2-mercaptoethyl)pyridinium chloride (preparation is given)

was hydrolyzed by refluxing in 6N HCl for 20 h under N, then the reaction mixture cooled and concentrated to obtain 3-(2,2-diphosphonoethyl)1-1(2-mercaptoethyl)pyridinium chloride (**I**). A capsule contained I 350.0, lactose 90.0, microcrystalline cellulose 60.0, and Mg stearate 1.0 mg. Phosphonate compounds were evaluated for bone resorption inhibition and mineralization in humans and animals, see abstract.

RN 154618-21-0 ZCAPLUS
CN Benzenaminium, 3-(2,2-diphosphonoethyl)-N,N,N-trimethyl-, inner salt (CA INDEX NAME)

10/511048



Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a

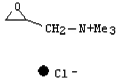
person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ali Vassem (WO 2000067708) in view of Aymard et al. (EP216681, presented in IDS).

The primary reference does not teach the specific species of bisphosphonate such as TMADP which is disclosed in instant specification.

Aymard et al. teach process for preparing cationic dispersing agents (title).Cationic dispersing agents (bisphosphonates) are prepared by the reaction of a compound containing OH and phosphono groups with a compound containing a quaternary N and a group reactive with phosphono groups. The dispersing agents are useful in the paper, textile, and coating industries. Treatment of 315 parts 55% aqueous 1-hydroxy-1,1-diphosphonoethane at 50° with 110 parts 2,3-epoxypropyltrimethylammonium chloride during 10 min, heating 2 h at 50°, and heating to 100-105° during 5 h gave 425 parts HOCMe[P(O)(OH)2]P(O)(OH)OCH2CH(OH)CH2N+Me3 Cl- which was used as a pigment dispersant in the manufacture of paper.

IT 3033-77-0, 2,3-Epoxypropyltrimethylammonium chloride
(esterification of, by hydroxyalkanediphosphonic acid)
RN 3033-77-0 HCAPLUS
CN 2-Oxiranemethanaminium, N,N,N-trimethyl-, chloride (1:1) (CA
INDEX
NAME)



IC ICM C07F009-40
ICS D21H003-02
CC 46-4 (Surface Active Agents and Detergents)
Section cross-reference(s): 23, 40, 42, 43
IT 2809-21-4, 1-Hydroxy-1,1-ethanediphosphonic acid 16856-53-
4,
1-Hydroxy-1,1-butanediphosphonic acid
(esterification of, by epoxypropyltrimethylammonium
halide)
IT 3033-77-0, 2,3-Epoxypropyltrimethylammonium chloride
13895-77-7
(esterification of, by hydroxyalkanediphosphonic acid)

The reference teaches preparation of the claimed TMADP compound and discloses TMADP's utility in textile, paper and coating industries as disclosed above (abstract and Chemical Registry No.) It is therefore apparent that water is utilized in textile and paper applications. Further the compound is a bisphosphonate and since primary reference teaches application of bisphosphonate in dental hygiene composition

and in removing dental calculus, It would have been obvious to one of ordinary skill to utilize the cationic dispersant which is also a bisphosphonate as taught by Aymard et al. in oral preparations of primary reference because the reference discloses application of bisphosphonates in dental plaque treating applications.

(Note: It is to be noted that applicants have not provided any specific species that represent hydrophilic group as substituent "A" in amended formula I as presented in claim 1).

Response to Arguments

11. Applicant's arguments with respect to claims have been considered but are moot in view of the new ground(s) of rejection.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/

Examiner, Art Unit 1612

/Gollamudi S Kishore/

Primary Examiner, Art Unit 1612